

## IN THE CLAIMS

Please delete all prior lists of claims and insert the following list of claims:

1. (CURRENTLY AMENDED) An *in vitro* method of evaluating one or more test compounds to identify test compounds that modulate binding of sequence-specific regulatory factors to corresponding single-, double-, or triple-stranded nucleic acid binding sites, the method comprising:

(a) providing an isolated nucleic acid target that defines ~~at least~~ one and only one known or putative binding site for a sequence-specific regulatory factor, the nucleic acid target having conjugated or covalently bonded thereto, at a point proximate to, but not within, the binding site:

(i) ~~an~~ one and only one anchor moiety,

(ii) a linker moiety covalently bonded to the anchor moiety, wherein the linker moiety is at least 30 Å long and is entropically destabilized such that entropy of the linker moiety confers temperature-sensitive, conditional behavior upon the isolated nucleic acid target, and

(iii) a test compound bonded to the linker moiety; and then

(b) under transcription conditions, contacting *in vitro* the nucleic acid target of step (a) to a reagent mixture comprising one or more sequence-specific regulatory factors specific for the binding site defined in the nucleic acid target; and then

(c) determining whether binding of the sequence-specific regulatory factor to the binding site defined in the nucleic acid target, and excluding measuring recruitment of non-sequence specific transcriptional machinery, is modulated by presence of the test compound.

2. (ORIGINAL) The method of Claim 1, wherein in step (a)(i), the anchor moiety comprises a polyamide or an intercalator.

3. (ORIGINAL) The method of Claim 1, wherein in step (a)(i), the anchor moiety comprises a moiety selected from the group consisting of a major-groove-binding/triple helix-forming oligonucleotide, a C<sub>1-6</sub> alkyl, a polycyclic aromatic hydrocarbon, a peptide nucleic acid, a polyamide, mitomycin C, cisplatin, and anthramycin.

4. (ORIGINAL) The method of Claim 1, wherein in step (a)(i), the anchor moiety is covalently bonded to the nucleic acid target.

5. (CANCELED)

6. (CURRENTLY AMENDED) The method of Claim ~~5~~ 1, wherein in step (a)(i), the anchor moiety comprises a moiety selected from the group consisting of a major-groove-binding/triple helix-forming oligonucleotide, a C<sub>1-6</sub> alkyl, a polycyclic aromatic hydrocarbon, an intercalator, a peptide nucleic acid, a polyamide, mitomycin C, cisplatin, and anthramycin.

7. (CURRENTLY AMENDED) The method of Claim ~~5~~ 1, wherein in step (a)(ii), the linker moiety comprises a bifunctional moiety selected from the group consisting of polypeptides, poly(ethyleneglycols), and C<sub>1-6</sub> alkylenyl, alkenyl, and alkynyl.

8. (ORIGINAL) The method of Claim 1, wherein in step (a)(ii), the linker moiety comprises a bifunctional moiety selected from the group consisting of polypeptides, poly(ethyleneglycols), and C<sub>1-6</sub> alkyl, alkene, and alkyne.

9. (ORIGINAL) The method of Claim 8, wherein in step (a)(i), the anchor moiety comprises a moiety selected from the group consisting of a major-groove-binding/triple helix-forming oligonucleotide, a C<sub>1-6</sub> alkyl, a polycyclic aromatic hydrocarbon, an intercalator, a peptide nucleic acid, a polyamide, mitomycin C, cisplatin, and anthramycin.

10. (ORIGINAL) The method of Claim 1, wherein in step (a)(ii), the linker moiety is an aptamer.

11. (CANCELED)

12. (CANCELED)

13. (CURRENTLY AMENDED) A method of evaluating one or more test compounds to identify test compounds that facilitate, recruit, or stabilize binding of sequence-specific natural transcription factors to corresponding single-, double-, or triple-stranded transcription factor binding sites on nucleic acid, the method comprising:

(a) providing an isolated nucleic acid target that defines ~~at least~~ one and only one desired sequence-specific transcription factor binding site, the nucleic acid target having covalently bonded thereto, at a point proximate to, but not within, the transcription factor binding site:

(i) an one and only one anchor moiety,

(ii) a linker moiety covalently bonded to the anchor moiety, wherein the linker moiety is at least about 30 Å long and is entropically destabilized such that entropy of the linker moiety confers temperature-sensitive, conditional behavior upon the isolated nucleic acid target, and

(iii) a test compound bonded to the linker moiety; and then

(b) under transcription conditions, contacting *in vitro* the nucleic acid target of step (a) to a reagent mixture comprising one or more sequence-specific natural transcription factors specific for the transcription factor binding site defined in the nucleic acid target; and then

(c) determining whether the test compound alters binding of the natural transcription factor to the nucleic acid target, and excluding measuring recruitment of non-sequence specific transcriptional machinery.

14. (CANCELED)

15. (CURRENTLY AMENDED) The method of Claim ~~14~~ 13, wherein in step (a)(i), the anchor moiety comprises a moiety selected from the group consisting of a major-groove-binding/triple helix-forming oligonucleotide, a C<sub>1-6</sub> alkyl, a polycyclic aromatic hydrocarbon, an intercalator, a peptide nucleic acid, a polyamide, mitomycin C, cisplatin, and anthramycin.

16. (CURRENTLY AMENDED) The method of Claim ~~14~~ 13, wherein in step

(a)(ii), the linker moiety comprises a bifunctional moiety selected from the group consisting of polypeptides, poly(ethyleneglycols), and C<sub>1-6</sub> alkylenyl, alkenyl, and alkynyl.

17. (ORIGINAL) The method of Claim 13, wherein in step (a)(ii), the linker moiety comprises a bifunctional moiety selected from the group consisting of polypeptides, poly(ethyleneglycols), and C<sub>1-6</sub> alkyl, alkene, and alkyne.

18. (ORIGINAL) The method of Claim 17, wherein in step (a)(i), the anchor moiety comprises a moiety selected from the group consisting of a major-groove-binding/triple helix-forming oligonucleotide, a C<sub>1-6</sub> alkyl, a polycyclic aromatic hydrocarbon, an intercalator, a peptide nucleic acid, a polyamide, mitomycin C, cisplatin, and anthramycin.

19. (ORIGINAL) The method of Claim 13, wherein in step (a)(ii), the linker moiety is an aptamer.

20. (CANCELED)

21. (CANCELED)

22. (CURRENTLY AMENDED) A method of evaluating one or more test compounds to identify test compounds that facilitate, recruit, or stabilize binding of sequence-specific transcription factors to corresponding single-, double-, or triple-stranded transcription factor binding sites on nucleic acid, the method comprising:

(a) providing an isolated nucleic acid target that defines ~~at least~~ one and only one desired sequence-specific transcription factor binding site, the nucleic acid target having covalently bonded thereto, at a point proximate to, but not within, the transcription factor binding site:

- (i) ~~an~~ one and only one anchor moiety,
- (ii) a linker moiety covalently bonded to the anchor moiety, wherein the linker moiety is at least about 30 Å long and is entropically destabilized such that entropy of the linker

moiety confers temperature-sensitive, conditional behavior upon the isolated nucleic acid target, and

(iii) a test compound bonded to the linker moiety, wherein the test compound is known to modulate binding of natural transcription factors to the transcription factor binding site defined in the nucleic acid target; and then

(b) under transcription conditions, contacting *in vitro* the nucleic acid target of step (a) to a reagent mixture comprising one or more known or putative transcription factors specific for the transcription factor binding site defined in the nucleic acid target; and then

(c) determining whether the test compound alters binding of the transcription factor to the nucleic acid target, **and excluding measuring recruitment of non-sequence specific transcriptional machinery.**

23. (CANCELED)

24. (CURRENTLY AMENDED) The method of Claim ~~23~~ 22, wherein in step (a)(i), the anchor moiety comprises a moiety selected from the group consisting of a major-groove-binding/triple helix-forming oligonucleotide, a C<sub>1-6</sub> alkyl, a polycyclic aromatic hydrocarbon, an intercalator, a peptide nucleic acid, a polyamide, mitomycin C, cisplatin, and anthramycin.

25. (CURRENTLY AMENDED) The method of Claim ~~23~~ 22, wherein in step (a)(ii), the linker moiety comprises a bifunctional moiety selected from the group consisting of polypeptides, poly(ethyleneglycols), and C<sub>1-6</sub> alkylenyl, alkenyl, and alkynyl.

26. (ORIGINAL) The method of Claim 22, wherein in step (a)(ii), the linker moiety comprises a bifunctional moiety selected from the group consisting of polypeptides, poly(ethyleneglycols), and C<sub>1-6</sub> alkyl, alkene, and alkyne.

27. (ORIGINAL) The method of Claim 22, wherein in step (a)(i), the anchor moiety comprises a moiety selected from the group consisting of a major-groove-binding/triple helix-forming oligonucleotide, a C<sub>1-6</sub> alkyl, a polycyclic aromatic hydrocarbon, an intercalator, a

peptide nucleic acid, a polyamide, mitomycin C, cisplatin, and anthramycin.

28. (ORIGINAL) The method of Claim 22, wherein in step (a)(ii), the linker moiety is an aptamer.

29. (CANCELED)

30. (CANCELED)

31. (CURRENTLY AMENDED) A composition of matter comprising an isolated nucleic acid target that defines ~~a~~ **one and only one** desired or putative binding site for a sequence-specific regulatory factor, **excluding binding sites for transcriptional machinery**, the isolated nucleic acid target having covalently bonded thereto, at a point proximate to the binding site, but not within the binding site, ~~an~~ **one and only one** anchor moiety, a linker moiety covalently bonded to the anchor moiety, wherein the linker moiety is at least about 30 Å long and is entropically destabilized such that entropy of the linker moiety confers temperature-sensitive, conditional behavior upon the isolated nucleic acid target, and a test compound conjugated to the linker moiety.

32. (PREVIOUSLY PRESENTED) The composition of matter of Claim 31, wherein the linker moiety is an aptamer.

33. (CANCELED)

34. (CURRENTLY AMENDED) A composition of matter comprising an isolated nucleic acid target that defines ~~a~~ **one and only one** desired or putative binding site for a sequence-specific regulatory factor, **excluding binding sites for transcriptional machinery**, the isolated nucleic acid target having covalently bonded thereto, at a point proximate to the binding site, ~~an~~ **one and only one** anchor moiety, a linker moiety covalently bonded to the anchor

moiety, and a test compound conjugated to the linker moiety, wherein the linker moiety is at least 30 Å long and entropically destabilized such that entropy of the linker moiety confers temperature-sensitive, conditional behavior upon the isolated nucleic acid target.

35. (CURRENTLY AMENDED) A kit for testing a compound for its ability to modulate binding of a sequence-specific regulatory factor to a corresponding sequence-specific regulatory factor binding site on a nucleic acid, the kit comprising:

an isolated nucleic acid target that defines a one and only one sequence-specific regulatory factor binding site, the isolated nucleic acid target further comprising ~~an~~ one and only one anchor moiety covalently bonded thereto at a point proximate to the regulatory factor binding site, but not within the regulatory factor binding site, and a bifunctional linker moiety covalently bonded to the anchor moiety, wherein the bifunctional linker moiety is at least about 30 Å long and comprises a free terminus that is dimensioned and configured to be conjugated to a compound to be tested; the isolated nucleic acid target being disposed in a suitable container, and

instructions for use of the kit.

36. (CURRENTLY AMENDED) A kit for testing a compound for its ability to modulate binding of a regulatory factor to a corresponding regulatory factor binding site on a nucleic acid, the kit comprising:

an isolated nucleic acid target that defines a one and only one regulatory factor binding site, the isolated nucleic acid target further comprising ~~an~~ one and only one anchor moiety covalently bonded thereto at a point proximate to the regulatory factor binding site, and a bifunctional linker moiety, wherein the bifunctional linker moiety is an aptamer, covalently bonded to the anchor moiety, wherein the bifunctional linker moiety comprises a free terminus that is dimensioned and configured to be conjugated to a compound to be tested; the isolated nucleic acid target being disposed in a suitable container, and

instructions for use of the kit.

37. (CANCELED)

38. (CURRENTLY AMENDED) A kit for testing a compound for its ability to modulate binding of a sequence-specific regulatory factor to a corresponding sequence-specific regulatory factor binding site on a nucleic acid, the kit comprising:

an isolated nucleic acid target that defines a one and only one sequence-specific regulatory factor binding site, the isolated nucleic acid target further comprising ~~an~~ one and only one anchor moiety covalently bonded thereto at a point proximate to the regulatory factor binding site, and a bifunctional linker moiety covalently bonded to the anchor moiety, wherein the bifunctional linker moiety is entropically destabilized such that entropy of the linker moiety confers temperature-sensitive conditional behavior upon the isolated nucleic acid target, and further wherein the bifunctional linker moiety comprises a free terminus that is dimensioned and configured to be conjugated to a compound to be tested; the isolated nucleic acid target being disposed in a suitable container, and  
instructions for use of the kit.